



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
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| <b>(51) International Patent Classification <sup>6</sup>:</b><br><b>C07D 239/95, A61K 31/505</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | <b>A3</b> | <b>(11) International Publication Number:</b> <b>WO 97/20823</b><br><b>(43) International Publication Date:</b> 12 June 1997 (12.06.97)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>(21) International Application Number:</b> PCT/EP96/05067<br><b>(22) International Filing Date:</b> 18 November 1996 (18.11.96)<br><b>(30) Priority Data:</b><br>08/566,378 1 December 1995 (01.12.95) US<br><b>(60) Parent Application or Grant</b><br><b>(63) Related by Continuation</b><br>US 08/566,378 (CIP)<br>Filed on 1 December 1995 (01.12.95)<br><b>(71) Applicant (for all designated States except US):</b> NOVARTIS AG [CH/CH]; Schwarzwaldallee 215, CH-4058 Basle (CH).<br><b>(72) Inventors; and</b><br><b>(75) Inventors/Applicants (for US only):</b> RÜEGER, Heinrich [CH/CH]; Alemannenweg 6, CH-4112 Flüh (CH). SCHMIDLIN, Tibur [CH/CH]; Friedensgasse 36, CH-4056 Basle (CH). RIGOLLIER, Pascal [FR/FR]; 2, rue Sainte-Catherine, F-68100 Mulhouse (FR). YAMAGUCHI, Yasuchika [JP/CH]; Tellstrasse 44/2, CH-4053 Basle (CH). TINTELNOT-BLOMLEY, Marina [DE/DE]; Rötterstrasse 1, D-79689 Maulburg (DE). SCHILLING, Walter [CH/CH]; Im Muspenacker, CH-4204 Himmelried (CH). CRISCIONE, |           | Leoluca [IT/CH]; Kirchstrasse 15, CH-4313 Möhlin (CH). MAH, Robert [CA/CH]; Baslerstrasse 258, CH-4123 Allschwil (CH).<br><b>(74) Common Representative:</b> NOVARTIS AG; Patent and Trade-mark Dept., Klybeckstrasse 141, CH-4002 Basle (CH).<br><b>(81) Designated States:</b> AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).<br><b>Published</b><br><i>With international search report.</i><br><i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i><br><b>(88) Date of publication of the international search report:</b><br>17 July 1997 (17.07.97) |
| <b>(54) Title:</b> 2-AMINO QUINAZOLINE DERIVATIVES AS NPY RECEPTOR ANTAGONISTS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <div style="text-align: center;"> </div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <b>(57) Abstract</b><br><p>The invention relates to a compound of formula (I) in which the variables are as defined and/or a salt or a tautomer thereof; and relates to a method of treatment of disorders or diseases associated with NPY receptor subtype Y5, to pharmaceutical compositions comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof and to the manufacture of the compounds of formula (I) or a salt thereof.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |

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## INTERNATIONAL SEARCH REPORT

Internat. Application No

PCT/EP 96/05067

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D239/95 A61K31/505

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                            | Relevant to claim No. |
|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X          | US 4 287 341 A (HESS ET. AL.) 1 September 1981<br>see example 18<br>---                                                                                                                                                                                                                                       | 1-5                   |
| X          | WO 92 07844 A (PFIZER INC.) 14 May 1992<br>see claims; example 85<br>---                                                                                                                                                                                                                                      | 1-3                   |
| X          | JOURNAL OF MEDICINAL CHEMISTRY,<br>vol. 36, no. 6, June 1993, WASHINGTON DC,<br>US,<br>pages 690-8, XP000652149<br>D. GIARDINA ET. AL.: "Structure-Activity<br>Relationships in Prazosin-Related<br>Compounds. 2. Role of the Piperazine Ring<br>on alpha-Blocking Activity. "<br>see table 1.<br>---<br>-/-- | 1-5                   |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search

6 May 1997

Date of mailing of the international search report

30.05.97

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

Internat. Application No.

PCT/EP 96/05067

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                      | Relevant to claim No. |
|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X          | JOURNAL OF MEDICINAL CHEMISTRY,<br>vol. 24, no. 2, February 1981, WASHINGTON<br>DC, US,<br>pages 127-40, XP000653661<br>E. F. ELSLAGER ET. AL.: "Synthesis and<br>Antimalarial Effects of<br>N2-Aryl-N4-[(dialkylamino)alkyl]- and<br>N4-Aryl-N2-[(dialkylamino)alkyl]-<br>2,4-quinazolinediamines."<br>see tables I-IV | 1-5                   |
| A          | ---<br>EP 0 614 911 A (ELF SANOFI) 14 September<br>1994<br>see whole document                                                                                                                                                                                                                                           | 1-12                  |
| A          | ---<br>EP 0 448 765 A (HEUMANN PHARMA GMBH) 2<br>October 1991<br>see whole document                                                                                                                                                                                                                                     | 1-12                  |
| P,A        | ---<br>WO 96 12489 A (ELI LILLY & CO.) 2 May 1996<br>see claims; examples<br>-----                                                                                                                                                                                                                                      | 1-12                  |

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 96/05067

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claim(s) 10  
is(are) directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☒ Claims Nos.: 1-7,9-12  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:  
Due to the very broad scope of the claims and the inclusion of vague  
definitions such as "heteroaryl", the search has been limited to the  
scope covered by the examples (Guidelines B-III, 3.7).
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Internat. Application No

PCT/EP 96/05067

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|-------------------------------------------|---------------------|----------------------------|---------------------|
| US 4287341 A                              | 01-09-81            | AR 227650 A                | 30-11-82            |
|                                           |                     | AU 520344 B                | 28-01-82            |
|                                           |                     | AU 6389680 A               | 07-05-81            |
|                                           |                     | CA 1146546 A               | 17-05-83            |
|                                           |                     | EP 0028473 A               | 13-05-81            |
|                                           |                     | US 4377581 A               | 22-03-83            |
|                                           |                     | US 4351940 A               | 28-09-82            |
|                                           |                     | JP 1438808 C               | 19-05-88            |
|                                           |                     | JP 56079676 A              | 30-06-81            |
|                                           |                     | JP 62043996 B              | 17-09-87            |
| WO 9207844 A                              | 14-05-92            | AT 124694 T                | 15-07-95            |
|                                           |                     | AU 644035 B                | 02-12-93            |
|                                           |                     | AU 9059291 A               | 26-05-92            |
|                                           |                     | BR 9107070 A               | 31-05-94            |
|                                           |                     | CA 2095213 A               | 07-05-92            |
|                                           |                     | CN 1061411 A               | 27-05-92            |
|                                           |                     | DE 9190155 U               | 07-10-93            |
|                                           |                     | DE 69111077 D              | 10-08-95            |
|                                           |                     | DE 69111077 T              | 02-11-95            |
|                                           |                     | EP 0556310 A               | 25-08-93            |
|                                           |                     | ES 2074867 T               | 16-09-95            |
|                                           |                     | FI 932032 A                | 05-05-93            |
|                                           |                     | HU 64533 A                 | 28-01-94            |
|                                           |                     | NZ 240476 A                | 27-04-94            |
|                                           |                     | SK 400992 A                | 09-08-95            |
|                                           |                     | US 5444062 A               | 22-08-95            |
|                                           |                     | ZA 9108767 A               | 05-05-93            |
| EP 614911 A                               | 14-09-94            | FR 2701480 A               | 19-08-94            |
|                                           |                     | AU 673398 B                | 07-11-96            |
|                                           |                     | AU 5516594 A               | 18-08-94            |
|                                           |                     | CA 2115631 A               | 16-08-94            |
|                                           |                     | CN 1104634 A               | 05-07-95            |
|                                           |                     | FI 940680 A                | 16-08-94            |
|                                           |                     | HU 66960 A                 | 30-01-95            |
|                                           |                     | JP 6293794 A               | 21-10-94            |
|                                           |                     | NO 940503 A                | 16-08-94            |
|                                           |                     | NZ 250878 A                | 27-02-96            |
|                                           |                     | US 5506258 A               | 09-04-96            |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP 96/05067

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|-------------------------------------------|---------------------|----------------------------|---------------------|
| EP 614911 A                               |                     | ZA 9401029 A               | 15-08-95            |
| EP 448765 A                               | 02-10-91            | AT 109979 T                | 15-09-94            |
|                                           |                     | AU 637882 B                | 10-06-93            |
|                                           |                     | CA 2037433 A               | 01-10-91            |
|                                           |                     | DE 59006842 D              | 22-09-94            |
|                                           |                     | IE 65252 B                 | 18-10-95            |
|                                           |                     | IL 97424 A                 | 26-05-95            |
|                                           |                     | JP 7089939 A               | 04-04-95            |
| WO 9612489 A                              | 02-05-96            | AU 3953795 A               | 15-05-96            |
|                                           |                     | EP 0716854 A               | 19-06-96            |

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